

Chapter 15: Alcohols, Diols, and Thiols

15.1: Sources of Alcohols (Table 15.1, p. 616)

Hydration of alkenes (Chapter 6)

1. Acid-catalyzed hydration (Chapter 6.6)
2. Oxymercuration (p. 258-9)
3. Hydroboration (Chapter 6.8)

Hydrolysis of alkyl halides (Chapter 8.1)
nucleophilic substitution

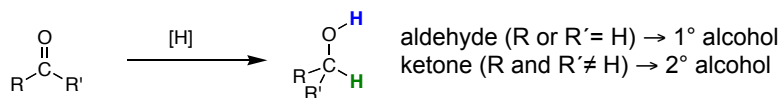
Reaction of Grignard or organolithium reagents with
ketones, aldehydes, and esters. (Chapter 14.5)

Reduction of aldehydes, ketones, esters, and
carboxylic acids (Chapters 15.2 - 15.3)

Reaction of epoxides with Grignard Reagents (Chapter 15.4)

Diols from the dihydroxylation of alkenes (Chapter 15.5)

15.2: Preparation of Alcohols by Reduction of Aldehydes and Ketones - add the equivalent of H_2 across the π -bond of the carbonyl to yield an alcohol

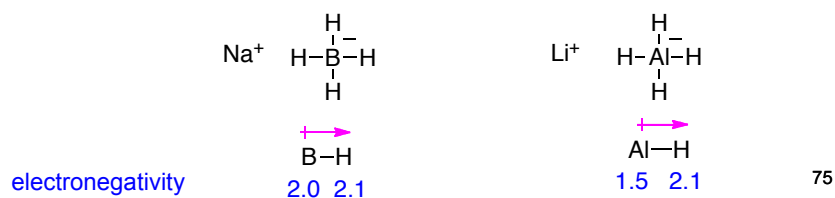


Catalytic hydrogenation is not typically used for the reduction of ketones or aldehydes to alcohols.

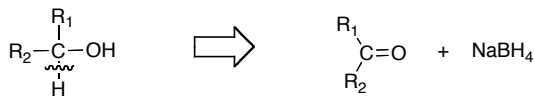
Metal hydride reagents: equivalent to $H:^-$ (hydride)

sodium borohydride
($NaBH_4$)

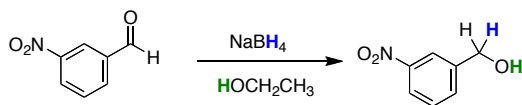
lithium aluminium hydride
($LiAlH_4$)



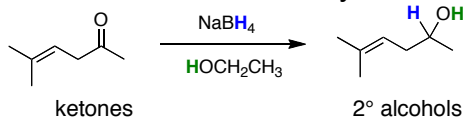
target disconnection precursors



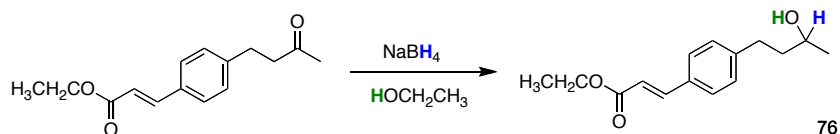
$NaBH_4$ reduces aldehydes to primary alcohols



$NaBH_4$ reduces ketones to secondary alcohols

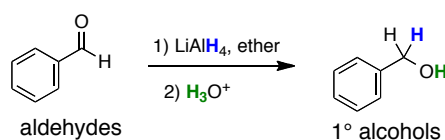
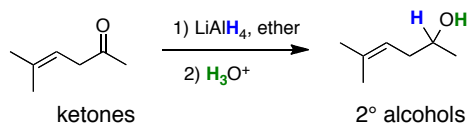


$NaBH_4$ does not react with esters or carboxylic acids



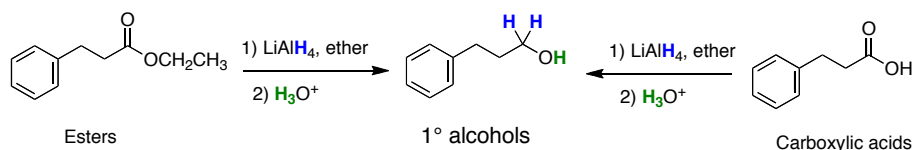
Lithium Aluminium Hydride (LiAlH_4 , LAH) - much more reactive than NaBH_4 . Incompatible with protic solvents (alcohols, H_2O).

LiAlH_4 (in ether) reduces aldehydes, carboxylic acids, and esters to 1° alcohols and ketones to 2° alcohols.

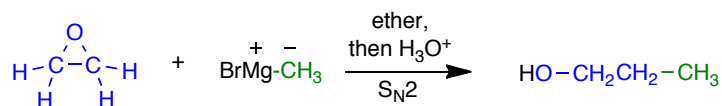


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15.3: Preparation of Alcohols By Reduction of Carboxylic Acids (and Esters) - LiAlH_4 (but not NaBH_4 or catalytic hydrogenation).

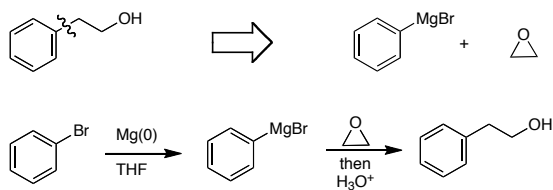


15.4: Preparation of Alcohols From Epoxides - the three-membered ring of an epoxide is strained. Epoxides undergo ring-opening reaction with nucleophiles (Grignard reagents, organolithium reagents, and cuprates).



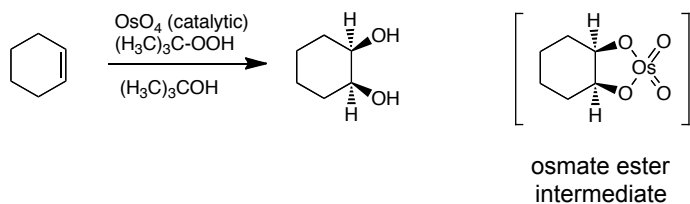
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target disconnection precursors



15.5: Preparation of Diols - Vicinal diols have hydroxyl groups on adjacent carbons (1,2-diols, *vic*-diols, glycols)

Dihydroxylation: formal addition of HO-OH across the π -bond of an alkene to give a 1,2-diol. This is an overall oxidation.



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15.6: Reactions of Alcohols: A Review and a Preview

Table 15.2, p.623

Conversion to alkyl halides (Chapter 4)

1. Reaction with hydrogen halides (Chapter 4.7)
2. Reaction with thionyl chloride (Chapter 4.12)
3. Reaction with phosphorous trihalides (Chapter 4.12)

Acid-catalyzed dehydration to alkenes (Chapter 5.9)

Conversion to *p*-toluenesulfonate esters (Chapter 8.11)

Conversion to ethers (Chapter 15.7)

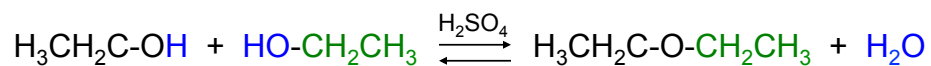
Conversion to esters (Chapter 15.8)

Oxidation to carbonyl compounds (Chapter 15.9)

Cleavage of vicinal diols to ketones and aldehydes
(Chapter 15.11)

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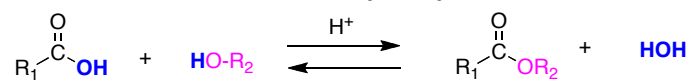
15.7: Conversion of Alcohols to Ethers - Symmetrical ethers can be prepared by treating the corresponding alcohol with a strong acid.



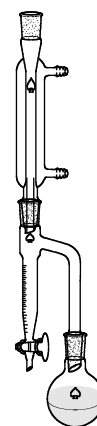
Limitations: ether must be symmetrical
works best for 1° alcohols

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15.8: Esterification - Fischer esterification: acid-catalyzed reaction between a carboxylic acid and alcohol to afford an ester. The reverse reaction is the *hydrolysis* of an ester



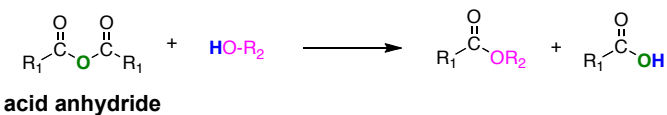
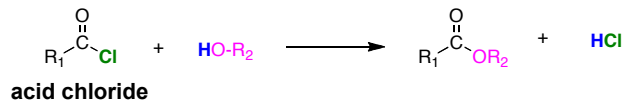
Mechanism (Chapters 18 and 19)



Dean-Stark
Trap

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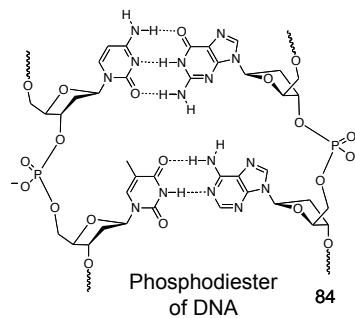
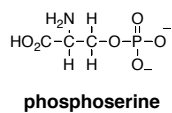
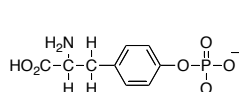
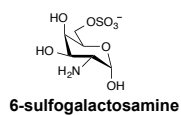
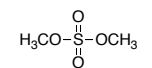
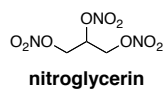
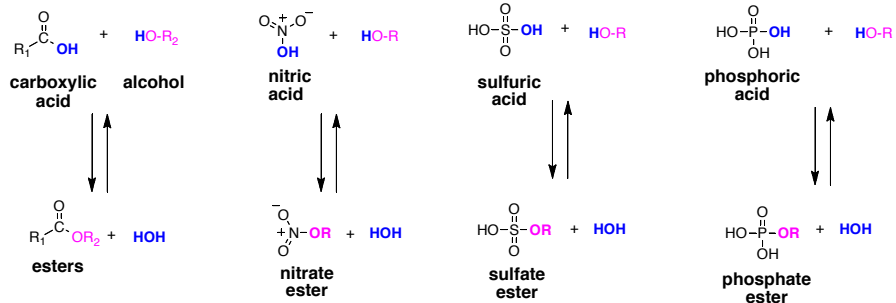
Ester formation via the reaction of an acid chloride or acid anhydride with an alcohol (nucleophilic acyl substitution)



Mechanism (Chapters 19)

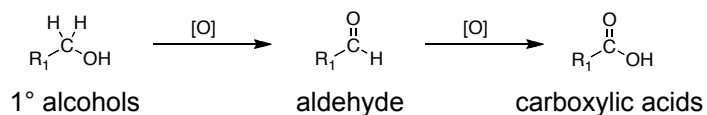
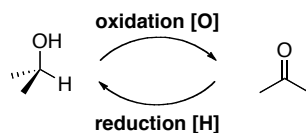
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Esters of Inorganic Acids



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15.9: Oxidation of Alcohols

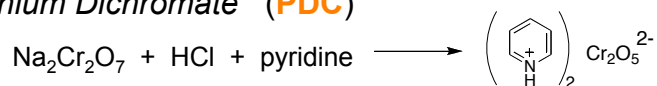


Potassium permanganate (KMnO_4) and **chromic acid** ($\text{Na}_2\text{Cr}_2\text{O}_7$, H_3O^+) oxidize secondary alcohols to ketones, and primary alcohols to carboxylic acids.

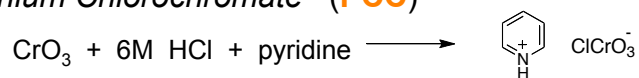
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Oxidation of primary alcohols to aldehydes

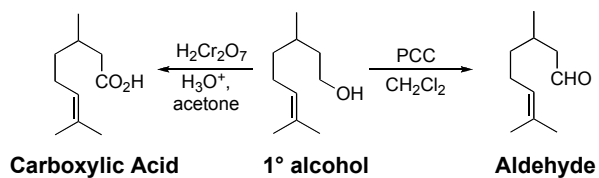
Pyridinium Dichromate (PDC)



Pyridinium Chlorochromate (PCC)

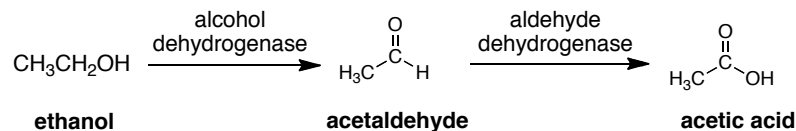


PCC and PDC are soluble in *anhydrous* organic solvent such as CH_2Cl_2 . The oxidation of primary alcohols with PCC or PDC in anhydrous CH_2Cl_2 stops at the aldehyde.

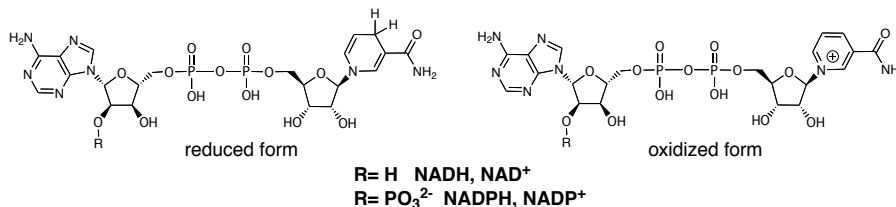


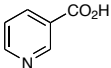
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15.10: Biological Oxidation of Alcohols (please read)
Ethanol metabolism:



Nicotinamide Adenine Dinucleotide (NAD)

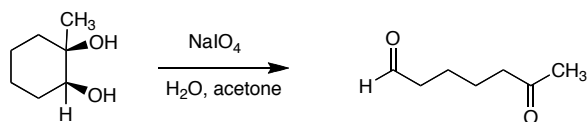
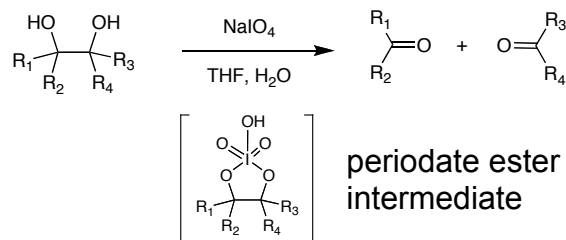


Vitamin B₃, nicotinic acid, niacin 

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15.11: Oxidative Cleavage of Vicinal Diols

Oxidative Cleavage of 1,2-diols to aldehydes and ketones with sodium periodate (NaIO_4) or periodic acid (HIO_4)

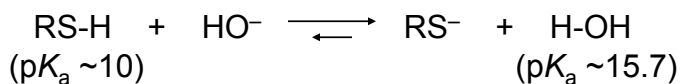


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15.12: Thiols

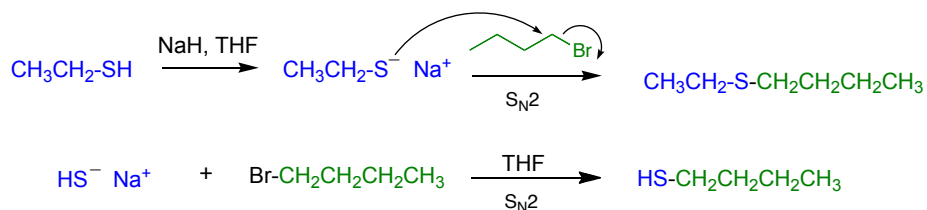
Thiols (mercaptans) are sulfur analogues of alcohols.

Thiols have a $pK_a \sim 10$ and are stronger acids than alcohols.



RS^- and HS^- are weakly basic and strong nucleophiles.

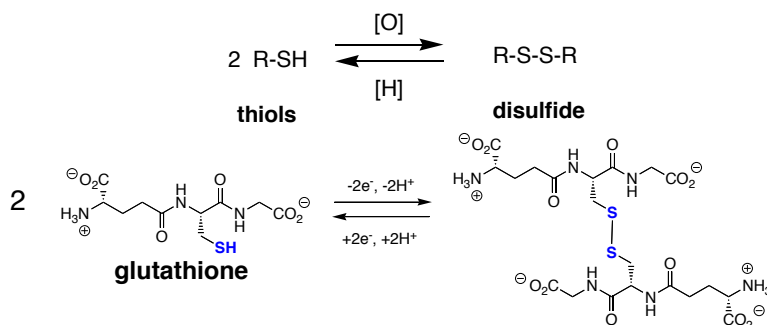
Thiolates react with 1° and 2° alkyl halides to yield sulfides ($\text{S}_{\text{N}}2$).



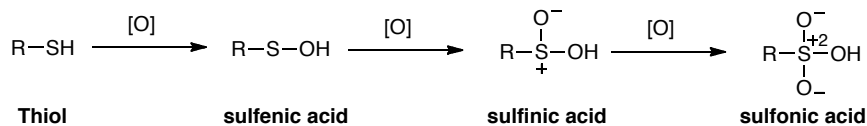
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Oxidation States of organosulfur compounds

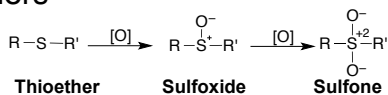
Thiols can be oxidized to disulfides



Oxidation of thiols to sulfonic acids

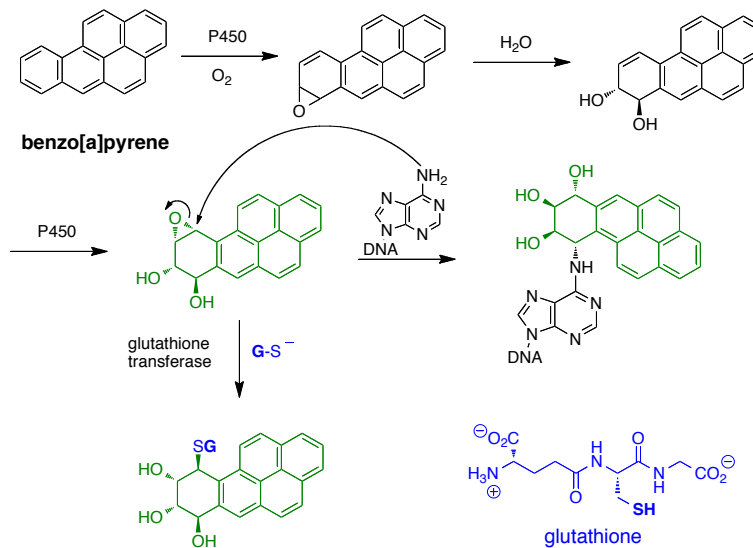


Oxidation of thioethers



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Bioactivation and detoxication of benzo[a]pyrene diol epoxide:



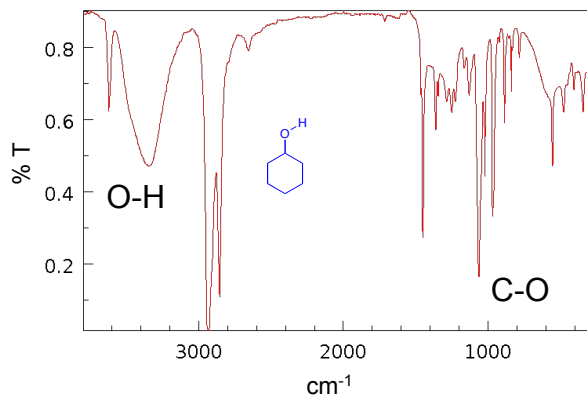
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15.13 Spectroscopic Analysis of Alcohols and Thiols:

Infrared (IR): Characteristic O–H stretching absorption at 3300 to 3600 cm⁻¹

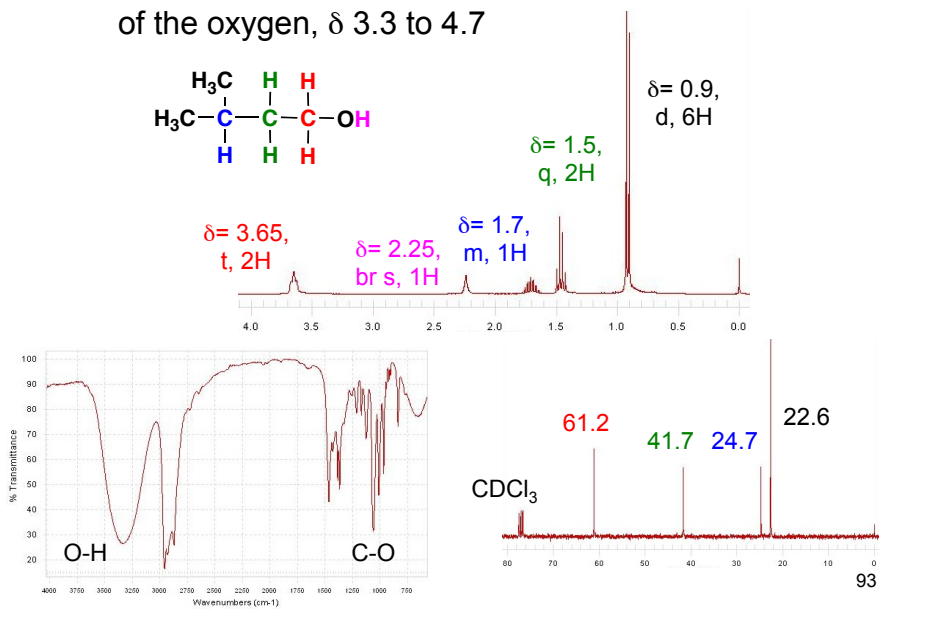
Sharp absorption near 3600 cm⁻¹ except if H-bonded: then broad absorption 3300 to 3400 cm⁻¹ range

Strong C–O stretching absorption near 1050 cm⁻¹

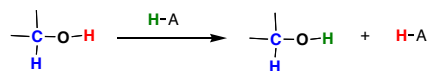


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^1H NMR: protons attached to the carbon bearing the hydroxyl group are deshielded by the electron-withdrawing nature of the oxygen, δ 3.3 to 4.7

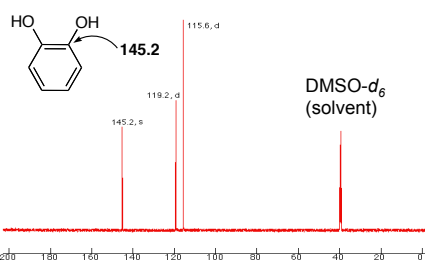
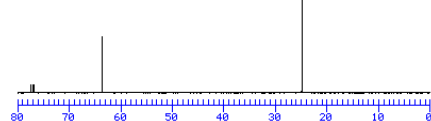
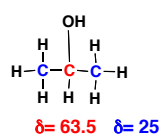
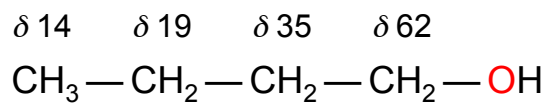


Usually spin-spin coupling is not observed between the O-H proton and neighboring protons on carbon due to exchange reaction



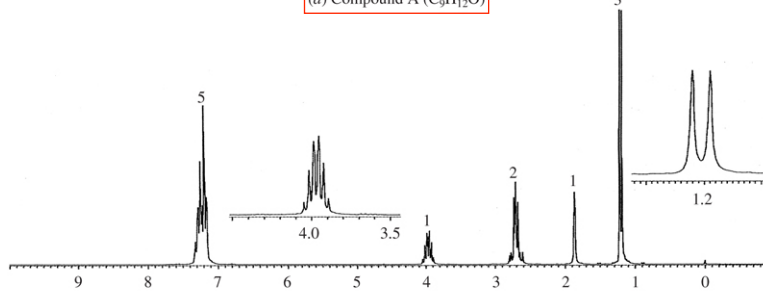
The chemical shift of the -OH proton occurs over a large range (2.0 - 5.5 ppm). Its chemical shift is dependent upon the sample concentration and temperature. This proton is often observed as a broad singlet (br s). Exchangable protons are often not to be observed at all.

^{13}C NMR: The oxygen of an alcohol will deshield the carbon it is attached to. The chemical shift range is 50-80 ppm

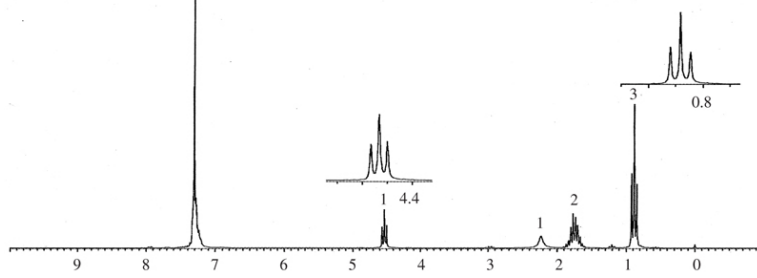


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(a) Compound A ($\text{C}_9\text{H}_{12}\text{O}$)



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(b) Compound B ($\text{C}_9\text{H}_{12}\text{O}$)



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Chemical shift (δ , ppm)